

When rapid onset and short duration of action are desired, 2-chloroprocaine (Nesacaine®) may be used. This ester-type local anesthetic is so rapidly hydrolyzed by plasma cholinesterase (half-life in venous blood of 21 seconds) that placental transfer of clinically significant amounts of drug is unlikely. Some anesthesiologists prefer to initiate an epidural block with 2-chloroprocaine, maintain the anesthesia with bupivacaine and then switch back to 2-chloroprocaine for the final perineal dose.

GERSHON LEVINSON, MD

#### REFERENCES

- Scanlon JW, Brown WW Jr, Weiss JB, et al: Neurobehavioral responses of newborn infants after maternal epidural anesthesia. *Anesthesiology* 40:121, Feb 1974
- Levinson G, Shnider SM: Placental transfer of local anesthetics: Clinical implications. In Marx G (Ed): *Parturition and Perinatology*. Philadelphia, F A Davis Co, 1973, pp 174-185

## Doses of Heparin and Protamine

HEPARIN REQUIREMENTS for cardiopulmonary bypass surgical procedures are usually calculated in milligrams or units of heparin per kilogram of body weight. However, this method of calculation may result in a seriously inappropriate dose of heparin due to wide differences between patients in their response to heparin and in the rate of its metabolic breakdown. Although variable response to drugs is common, heparin is exceptional because during surgical operation on the heart, inadequate heparinization can lead to serious, sometimes life-threatening coagulopathies.

At Loma Linda University the anticoagulant effect of heparin and its decay rate have been studied in 50 patients in whom cardiopulmonary bypass was done by measuring the activated coagulation time (ACT) of whole blood. To produce the desired activated coagulation time of eight minutes, the required loading dose of heparin differed by a factor of 3, with a range of 3.2 to 9.0 mg per kg of body weight. In the same group of patients, the half-life of heparin differed by a factor of 5, ranging from 0.8 to 4.5 hours.

This wide variability between patients insures that when the commonly used dose protocols are applied to a series of patients, some will be inadequately heparinized and others will receive much more heparin than they need.

Allowance for variations in patient response to

heparin can be provided by constructing a dose-response curve from ACT measurements. Such a curve relates the clotting time to heparin dose in each patient and permits the calculation of the heparin dose required. At the completion of bypass the same dose-response curve can be used to determine how much heparin activity remains in the patient, and consequently the amount of protamine required to neutralize it.

The determination of activated coagulation time is a simple test that can be done in the operating room by relatively unskilled personnel. It permits accurate control of heparin doses and subsequent neutralization with protamine, removing the guesswork from a procedure in which a bad guess can be disastrous.

BERNARD BRIGGS, MD

#### REFERENCES

- Bull BS, Korpman RA, Huse WM, et al: Heparin therapy during extracorporeal circulation. I—Problems inherent in existing heparin protocols. *J Thorac Cardiovasc Surg* 69:674-684, May 1975
- Bull BS, Huse WM, Brauer FS, et al: Heparin therapy during extracorporeal circulation. II—The use of dose-response curve to individualize heparin and protamine therapy. *J Thorac Cardiovasc Surg* 69:685-689, May 1975

## Ketamine

KETAMINE is an anesthetic agent that was introduced several years ago with much fanfare. Initial claims for the drug were grossly exaggerated and appeared in general circulation newspapers and magazines in addition to the medical literature. Now, after the initial wave of overenthusiasm as well as a backlash phase, it seems appropriate to consider what ketamine can and cannot do.

It is clear that even though laryngeal and pharyngeal reflexes often are not depressed or not notably depressed, ketamine cannot be given safely to every patient with a full stomach without danger of vomiting and aspiration of vomitus. There have been reports of patients who did vomit and aspirate after the drug was given. Nevertheless, there is some value in the relative sparing of laryngeal and pharyngeal reflexes. Ketamine is a potent analgesic agent and does produce anesthesia. It may be useful given alone or with other agents for certain kinds of procedures. These include (1) neurodiagnostic procedures such as myelograms, ventriculograms and pneumoencephalograms where the increase in the intracranial pressure produced by ketamine is not detrimental to the patient and

(2) debridement, painful dressing changes and skin grafting, particularly in burn patients. Other situations in which ketamine may be used include diagnostic and operative procedures of the pharynx, larynx, head, eye, ear, nose, anus and mouth (if given with other agents); and certain gynecologic procedures such as dilatation and curettage. Some physicians use ketamine for cardiac catheterization, or when anesthesia must be administered intramuscularly because an intravenous site is not available. It also may be valuable as an induction agent or indicated in poor risk patients or in orthopedic procedures such as closed reductions or manipulations.

The use of ketamine has several drawbacks. One is the apparent ease with which the drug may be administered intravenously or intramuscularly for the production of general anesthesia. This has resulted in administration of ketamine by unqualified persons under adverse circumstances, without adequate knowledge of resuscitation procedures or adequate equipment available. Another drawback is increased intracranial pressure and increased arterial pressure, which may be detrimental to some patients. The drug should be used only by those skilled in respiratory and circulatory support. Another problem with ketamine is the high incidence of untoward reactions on emergence from the drug. These include hallucinations and emergence delirium, including confusion, excitement and irrational behavior. Some patients recall these sensations as extremely unpleasant and request that they never again receive this drug. The frequency with which these emergence reactions occur is said to be approximately 12 percent. Appropriate premedication with a tranquilizer may minimize the frequency of emergence delirium and diminish its magnitude. Careful attention to the circumstances under which the patient awakens, including minimal stimulation, is believed also to diminish the frequency and severity of emergence complications, but it may be dangerous for patients to be allowed to recover in darkened seclusion.

Recently the use of low-dose ketamine (that is  $\frac{1}{4}$  to  $\frac{1}{2}$  mg per kg of body weight given intravenously, compared with 2 mg or more per kg of body weight given intramuscularly) has become of great interest. The available evidence suggests that emergence delirium is absent with low-dose techniques. However, additional studies are needed before this claim can be accepted with certainty.

In summary, ketamine is a valuable drug that is neither as good as enthusiasts nor as bad as its

detractors claim. Each anesthesiologist must work with ketamine and after appropriate experience decide what role it will have in his practice.

RONALD L. KATZ, MD

#### REFERENCE

Wilson RD: Current status of ketamine, chap 12, *In* Hershey SG (Ed): *The American Society of Anesthesiologists Regional Refresher Courses in Anesthesiology*. Highland Park, Ill. Lippincott Co., Vol 1. 1973, pp 157-167

## Present Status of Muscle Relaxants and Antagonists

MODERN SURGERY has benefited significantly from the introduction of neuromuscular blocking agents. Curare (d-tubocurarine) has been used clinically since the 1940's with generally satisfying results. While maintenance of skeletal muscle relaxation during surgical operation in most instances has been carried out successfully with this agent, for endotracheal intubation and for shorter surgical procedures a muscle relaxant with rapid onset and short duration of action is required. Succinylcholine, a synthetic agent introduced in 1951, fulfilled some of the requirements and was widely used. Significant side effects, however, may occur with each of these agents.

The shortcomings of d-tubocurarine are: (a) hypotension due to ganglionic blockade and occasional histamine release with associated skin reactions or rarely bronchial spasm, or both, and (b) relatively slow onset and long duration of action—the latter necessitating the frequent use of reversing agents of the anticholinesterase type (such as neostigmine and pyridostigmine). Clinical problems with succinylcholine are entirely different. This agent is not amenable to pharmacological reversal and its depolarizing action on the motor end-plate produces muscle fasciculations and muscle pains. Its duration of action depends on the rate of inactivation by plasma cholinesterase. Deficiency or abnormality of this enzyme and accidental overdose of the agent may produce extremely long lasting paralysis for which artificial ventilation is the only effective measure. Increased intraocular pressure, dysrhythmias, cardiac conduction abnormalities due to potassium release, post-operative myalgia and possibly very injurious hyperthermia are additional drawbacks to the use of succinylcholine. For these reasons research continued for new and superior muscle relaxant agents.

In the United States, gallamine, a curare-like